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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,336	08/20/2001	Neil James Butt	7174555913	6843
21874	7590	07/26/2004	EXAMINER	
<b>EDWARDS &amp; ANGELL, LLP</b> P.O. BOX 55874 BOSTON, MA 02205				MARVICH, MARIA
		ART UNIT		PAPER NUMBER
				1636

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/856,336	BUTT ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 19 April 2004.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1,3-35 and 37-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1,3-26,28-33,37-42,45 and 46 is/are rejected.
- 7) Claim(s) 27,34,35,43,44 and 47 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

This office action is in response to an amendment filed 4/19/04. Claims 2 and 36 has been cancelled and claims 45-47 have been added. Claims 1, 3, 13, 14 and 25 have been amended. Claims 1, 2-35 and 37-47 are pending.

### ***Response to Amendment***

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are new grounds of rejection herein that were not necessitated by applicants' amendment and therefore, this action is non-final.

### ***Priority***

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in the U.K. on 17 November 1998. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 3-12, 15-23 and 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This rejection is maintained for reasons of record in the office action mailed 11/17/03 and restated below. Upon reconsideration, the rejection has been extended to claims 15-23 and 37-40.**

Claims 1 and 37 are vague and indefinite in that the metes and bounds of the word “substantially” are unclear. The term “substantial” is a relative one not defined by the claim, no single set of conditions is recognized by the art as being “substantial” and because the specification does not provide a standard for ascertaining the requisite degree.

*Response to Amendment*

Applicants traverse the claim rejections under 35 U.S.C. 112, second paragraph on pages 14-16 of the amendment filed 4/19/04. Applicants argue that “substantially” appears in the claims of numerous U.S. patents. Secondly, the word “substantial” is defined according to Webster’s Ninth Collegiate Dictionary (1990). Thirdly, the use of a word such as substantially or the like may be inferred from the description of results of Example 1. In this example, separation conditions were evaluated as “OK”, “Good” and “Poor”. Applicants argue that even for separation conditions that do not result in absolute sequestration of the plasmid DNA in the organic phase, the methods may be of some use. The differences between plasmid DNA and genomic DNA can be evaluated on agarose gels, which would enable the practitioner of

the present invention to observe whether the plasmid DNA was “substantially” in one fraction and genomic DNA in the other.

Applicants’ argument filed 4/19/04 has been fully considered but they are not persuasive. As to the patentability of the instant case in light of similar claims in published patents that possess similar disclosures, rejections based upon this argument have been addressed in *in re* Giolito and Hoffman. “It is immaterial whether similar claims have been allowed to others” (see *in re* Giolito and Hoffman 188 USPQ 645). Rather, each application is reviewed on its own merits. It is not disputed that the word “substantially” has a definition nor that the specification provides guidance for the evaluation of DNA concentrations in the particular phases. Rather, the term “substantial” is a relative and no single set of conditions is recognized by the art as being “substantial”. Establishing “substantial” amounts of DNA in a given phase that amount that will satisfy the limitation of the claim that it be “substantial” is open to interpretation by the practitioner.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-7, 9-23, 25-26, 37-40 and 45-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the

time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Applicants claim a method for isolating plasmid DNA from genomic DNA “under conditions to denature genomic DNA”. Specifically, applicants claim use of a genus of basic conditions and bases to denture the DNA.

Applicants claim a genus of precipitating agents comprising alcohol.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

Applicants teach that the instantly claimed invention distinguishes itself from the prior art by minimizing steps required for the isolation of plasmid DNA from genomic DNA by the exploitation of the differential solubility between the two types of DNA under denaturing conditions. Following denaturation, in the presence of an extraction mixture comprised of chaotrope, butanol and water, genomic DNA separates into aqueous phases and plasmid DNA into butanol phase. Therefore, as an essential element, the invention claims a “condition” in which genomic DNA is denatured and can be retained in the aqueous phase of the extraction mixture while the plasmid DNA selectively migrates into the butanol phase. In the instant specification, we are only taught that appropriate conditions for denaturation are high temperature of 65°C or higher

for several minutes or basic conditions in which base is present. The disclosure of the afore stated conditions is not accompanied by a disclosure as to the relative properties of the condition that denatures DNA for retention in aqueous phases and yet allows plasmid DNA to migrate into the butanol phase. Therefore, there is no actual reduction to practice or clear description of what is required for "conditions to denture genomic DNA" to meet the limitations of the instant invention. Given the diversity of conditions that denature DNA and the inability to determine which will also meet the limitations of the instant invention, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of two species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Furthermore, while applicants claim a genus of basic conditions, and a genus of bases to be used to denature the DNA, applicants only teach use of NaOH. Specifically, sodium hydroxide at concentrations of 90 mM to 200 mM is shown to be adequate for "good" plasmid recovery (page 6-7, table). There is no actual reduction to practice or clear description of what is required to denature genomic DNA to meet the limitations of the instant invention. For example, it is known that water can act as a weak base. Is this adequate as a component of the extraction mixture? Given the diversity of bases and the inability to determine which will also meet the limitations of the instant invention, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Applicants teach that a precipitating agent such as alcohol can be used in the recovery step of the instant invention. The use of any alcohol as a precipitating agent is not disclosed in the prior art or the specification. Rather, the specification teaches the use of ethanol as a precipitating agent. Applicants have not reduced to practice or clearly described in pictures or descriptions the species of alcohols that would function as ethanol does precipitate the DNA. Applicants have not provided relevant identifying characteristics of ethanol such that any alcohol could be used as a precipitating agent. Given the unpredictability of the art and the inability to determine what type of alcohol will precipitate DNA versus for example function in extraction mix, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

***Response to Amendment***

Applicants traverse the previous claim rejections under 35 U.S.C. 112, first paragraph on pages 16-19 of the amendment filed 4/19/04. Applicants argue in their response essentially that pages 2-3 of the specification teaches a wide range of conditions for the denaturation of genomic DNA and that other conditions for denaturing DNA are well known in the art. Furthermore, applicants argue that they need not be limited to those conditions for which working examples have been provided. Finally, applicants state that the unpredictable art of denaturing conditions is unclear.

The arguments filed 4/19/03 in response to similar grounds of rejection have been considered but are not persuasive. The specification teaches that the DNA material is

mixed with reagents to denature the genomic DNA whereby the plasmid DNA is partitioned into an organic phase and the genomic DNA is partitioned into the aqueous phase (bridging paragraph page 2-3). Therefore, it is not enough to just denature the DNA. Rather differential solubility of plasmid and genomic DNA under denaturing conditions is an essential element required of the denaturing conditions. The specification teaches denaturation by elevated temperatures at 65°C or greater or addition of base preferably sodium hydroxide (page 3, line 2-16). This disclosure does not constitute written description for the identification of any condition required to denature the DNA such that the plasmid DNA migrates into the organic phase and the genomic DNA into the aqueous. Adequate written description requires more than a mere statement that the condition is part of the invention and a reference to a potential means of finding this condition. As to the unpredictable nature of the art, it is the identification of conditions in which the DNAs are partitioned into their respective phases that is unpredictable. Taken in total, the rejection states “(g)iven the diversity of conditions that denature DNA and the inability to determine which will also meet the limitations of the instant invention”, the art can be considered to be unpredictable.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 24-25, 29-33, 41-42 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Colpan et al (US 6,383,393 B1; see entire document). **This is a new rejection.**

Colpan et al teaches methods for the purification of nucleic acids such as the isolation of plasmid of cosmid DNA from *E. coli* using an aqueous solution (column 2, line 1-10 and line 63-67). For the extraction of the DNA, the aqueous solution comprises high concentrations of chaotropic salts used in combination with aliphatic alcohols with a chain length of 1 to 5 carbon atoms (see e.g. column 4, line 66 through column 5, line 5). Specifically recited for use in the aqueous chaotropic solution is butanol (see e.g. column 5, line 20-27). Water is a weak base and is an essential element of the extraction mixture taught by Colpan et al.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (US 6,383,393 B1; see entire document) in view of Sawadogo and Dyke (NAR, 1991, Vol 19(3), page 674; see entire document). **This is a new rejection.**

Applicants claim an extraction mixture which comprises butanol, a chaotrope, and water. Butanol is n-butanol, 2-methylproponal or butan-2-ol.

The teachings of Colpan et al are described above and are applied as before except; Colpan et al do not teach that Butanol is n-butanol, 2-methylproponal or butan-2-ol.

Sawadogo and Dyke teach the use of n-butanol in the extraction of oligonucleotides (see e.g. column 1, paragraph 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the butanol taught by Colpan et al with the n-butanol taught by Sawadogo and Dyke because Colpan et al teach that it is within the ordinary skill of the art to use butanol in an extraction mixture and because Sawadogo and Dyke teach that it is within the ordinary skill of the art to use n-butanol for extraction of DNA. One would have been motivated to do so in order to receive the expected benefit of reduced organic contaminants following use of n-butanol (Sawadogo and Dyke, page 674, column 1, paragraph 3). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

### *Conclusion*

Claims 1, 3-26, 28-33, 37-42 and 45-46 are rejected.

Claims 27, 34-35, 43-44 and 47 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD  
Examiner  
Art Unit 1636

July 20, 2004

  
GERRY LEFFERS  
PRIMARY EXAMINER